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EXAMINER

SCHNIZER, HOLLY G

ART UNIT PAPER NUMBER

1653

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/031,947

Applicant(s)

GAYED, ATEF

Examiner

Holly Schnizer

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 15 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-72 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-72 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 12-15-03 & 1-7-03.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Status of the Claims***

Claims 1-72 are pending and have been considered in this Office Action.

### ***Information Disclosure Statement***

The information disclosure statements filed January 7, 2003 and December 15, 2003 fail to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. In the instant case, copies of references D6, D7, and D8 in the IDS filed January 7, 2003 were not found in the application. The IDS indicates that copies were submitted with the provisional application. However, the copies were not found in the provisional application. References D7 and D8 were obtained by the examiner and considered. However, attempts to obtain reference D6 were not successful—the reference having the provided volume, date, author and page numbering could not be found. Applicant is advised to check the reference for this citation. Copies of references D9 and D10 of the IDS filed December 15, 2003 were also not found and thus have not been considered.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1653

Claims 50-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 50 recites the limitation "The vial of claim 1" in line 1. There is insufficient antecedent basis for this limitation in the claim since claim 1 is drawn to a composition and does not recite a vial. Claim 51 is unclear since it is dependent from Claim 50 and is also drawn to a vial. The claims are unclear as to whether a composition or vial is being claimed.

Claims 4-15 and 23-33 are rejected because they are unclear as to whether the percentage is by weight or by molar concentration.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 23-27, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Kakimoto et al. (EP 0 199 992 ; ref. B1 of IDS filed 1-7-03).

The examiner notes that the claimed compositions have been considered as to whether the prior art teaches a composition containing the same components and not as to how the composition is used (unless that use changes its physical components). Benzethonium chloride is the only recited component of the claimed compositions.

Therefore, even though the composition is to be used as a carrier of erythropoietin, without a recitation that erythropoietin is part of the composition, the claims have been interpreted to encompass compositions containing benzethonium chloride alone. Kakimoto et al. teaches a composition comprising 0.001% to 1% benzethonium chloride, a range that encompasses the ranges of Claims 23-27. Kakimoto et al. also teaches that the compositions described therein may also include a buffer (p. 9, lines 4-15). Thus, the compositions of Kakimoto et al. appear to be patentably indistinguishable from those of present claims 20, 23-27, and 34.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Nomura et al. (EP 0 459 795 ; ref. B2 of IDS filed 1-7-03).

Nomura et al. teaches a composition comprising EPO and benzethonium chloride (p. 4, lines 45-54). Nomura et al. teaches that the composition contains between 0.1 and 1000 parts by weight to one part by weight EPO which would be effective to inhibit microbial growth.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 4, 5, 7, 8, 16-20, 23, 24, 26, 27, 34-35, 50-54, 57-61, and 69-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strickland et al. (U.S.P

5,661,125; cited as D5 in IDS filed 1-7-03) in view of Uda et al. (U.S.P 5, 554, 378) and Sandeep et al. (PDA J. Pharm. Sci. Technol. 1997 51(4): 166-171).

Strickland et al. teach a multidose erythropoietin composition containing preservatives. The preferred preservatives include benzalkonium chloride (Col. 5, line 62). Strickland et al. indicate that the compositions can be maintained in vials for up to two years or more under both refrigerated conditions and controlled room conditions (Col. 4, lines 57-60).

Strickland et al. do not include benzethonium chloride as a preferred preservative.

Uda et al. provides evidence that one of skill in the art would have considered benzethonium chloride a functional equivalent of benzalkonium chloride and other preservatives listed in Strickland et al. (Col. 6, lines 28-35). Uda et al. also provides evidence that one of skill in the art would have considered benzethonium chloride a suitable preservative for use with erythropoietin (Col. 3, line 63) as erythropoietin is disclosed as one of the proteins that can be used in the disclosed compositions.

Sandeep et al. provides evidence that concentrations of benzethonium chloride that were at least 0.01% were routinely used in antimicrobial preservatives at the time of the invention (See. P. 168, Col. 2 and Table V).

It would have been obvious to one of ordinary skill in the art at the time of the invention to add a preservative to erythropoietin multi-dose solutions as disclosed in Strickland et al., wherein the preservative selected was benzethonium chloride in concentrations of at least 0.01% as disclosed in Sandeep et al. The selection of a

Art Unit: 1653

known material based on its suitability for its intended use supports the determination of prima facie obviousness. (see MPEP 2144.07 and also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945) cited therein). In the present case, Uda et al. and Sandeep et al. provide evidence that benzethonium chloride was a well known antimicrobial preservative. Strickland et al. provides evidence that using antimicrobial preservatives in erythropoietin multi-dose solutions was well known at the time of the invention. Both benzalkonium chloride (disclosed as an example of a preservative to use in erythropoietin solutions in Strickland et al.) and benzethonium chloride were considered functionally equivalent, as evidenced by Uda et al. Thus, the claims are considered obvious over Strickland et al. in view of Uda et al. and Sandeep et al.

Claims 2-3, 6, 9-15, 21-22, 25, 28-33, 36-49, 55-56, and 62-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strickland et al. (U.S.P 5,661,125; cited as D5 in IDS filed 1-7-03), Uda et al. (U.S.P 5, 554, 378) and Sandeep et al. as applied to claims 1, 4, 5, 7, 8, 16-20, 23, 24, 26, 27, 34-35, 50-54, 57-61, and 69-72 above, and further in view of Hyman et al. (U.S. Patent No. 3,489,837; ref. D1 of IDS filed 12-15-03).

The teachings of Strickland et al., Uda et al., and Sandeep et al. have been described above. Sandeep et al. teaches that benzethonium chloride and phenoxyethanol were well known preservatives (p. 168, Table V). Uda et al. teaches that benzethonium chloride and phenylethyl alcohol were well known preservatives

Art Unit: 1653

(Col. 6, lines 29-31). Thus, these references provide evidence that benzethonium chloride, phenoxyethanol, and phenyl ethyl alcohol were all well known preservatives at the time of the invention.

Hyman et al. teaches that when a composition is made containing benzethonium chloride with another preservative, a synergistic reaction occurs which provides much greater inhibition of the growth of E. coli than when using a single preservative (Col. 1, line 70-Col. 2, lines 1-5).

It would have been obvious to one of ordinary skill in the art at the time of the invention, to add a second preservative such as phenoxyethanol or phenyl ethyl alcohol to a erythropoietin solution so that the concentration of each preservative could be reduced as taught in Hyman et al. It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. (MPEP 2144.06). In the present case, benzethonium chloride, phenoxyethanol, and phenyl ethyl alcohol were all well known preservatives at the time of the invention and Hyman et al. teaches that combining benzethonium chloride with another preservative produces a synergistic reaction that provides much greater inhibition to bacterial growth. The selection of a known material (benzethonium chloride, phenoxyethanol, and phenyl ethyl alcohol) based on its suitability for its intended use (preservatives) supports the determination of prima facie obviousness. (see MPEP 2144.07 and also *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945) cited therein).



Art Unit: 1653

Thus, the claims are considered obvious over Strickland et al. in view of Uda et al..

Sandeep et al., and Hyman et al.

Claims 1, 4-8, 16-19, 35, 38-42, and 50-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kakimoto et al. (EP 0 199 992; ref. B1 of IDS filed 1-7-03) in view of Shimoda et al. (U.S. Patent No. 4,879,272) .

Shimoda et al. teaches that the adsorption of erythropoietin on the glass or plastic containers was a recognized problem in the art at the time of the invention (Col. 1). Shimoda et al. teaches a variety of additives that can be added to erythropoietin compositions to reduce the adsorption to the containers.

Shimoda et al. do not teach that benzethonium chloride can be used to prevent adsorption of erythropoietin to the walls of a container.

Kakimoto et al. teaches that adding 0.001% to 1% benzethonium chloride to pharmaceutical compositions prevents proteins from being adsorbed on the inner wall of the container that holds the composition (p. 6, line 10-p.7, line 19). Kakimoto et al. teaches that the methods disclosed therein can be used to prevent the effects against any peptide which tends to adsorb on container walls and is not limited to any protein or peptide (p. 6, lines 1-5).

Uda et al. provides evidence that at the time of the invention, those of ordinary skill in the art recognized that benzethonium chloride could be added to aqueous solutions as a preservative (Col. 6, lines 28-35).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the composition disclosed in Shimoda et al. by adding benzethonium

Art Unit: 1653

chloride to the erythropoietin composition, a known additive that would prevent protein adsorption on the wall of the container as taught in Kakimoto et al.. One of ordinary skill would have been motivated to choose benzethonium chloride over the additives taught in Shimoda et al. because 1) benzethonium chloride appears to be more effective at lower concentrations than the additives disclosed in Shimoda et al. (compare Figs. 1-10 of Kakimoto et al. to the Table in Col. 4 of Shimoda et al.) and 2) benzethonium chloride has the added benefit of acting as a preservative as taught in Uda et al.


### **Conclusions**

No Claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-0958. The examiner can normally be reached on Tuesday, Thursday, and Friday from 8 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Holly Schnizer  
May 13, 2004

  
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